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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/975,317	10/12/2001	Alan David Watson	WATS3001/REF/C	8178

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EXAMINER	
HARTLEY, MICHAEL G	
ART UNIT	**PAPER NUMBER**
1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/975,317	Applicant(s) WATSON ET AL.	
	Examiner Michael G. Hartley	Art Unit 1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 August 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *51-74* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *51-74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Response to Amendment

The amendment filed 8/23/2003 has been entered. Claims 1-50 have been canceled. New claims 51-74 have been added.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 51-53, 55-58 and 64-74 are rejected under 35 U.S.C. 102(b) as being anticipated by Ericcson (WO 95/02831, US 5,869,023 used as a US equivalent).

Ericcson discloses a method of detecting myocardial ischemia in a subject comprising administering a physiologically acceptable manganese complex at a dosage within the claimed range (see column 7, lines 62-65) and subjecting the body to MRI (as claimed, i.e., echo planer) and providing a series of images to identify regions of abnormal blood flow (e.g., an infarction), see examples 4-6, which discloses various methods of imaging myocardial ischemia, as claimed, including determining the severity (column 6, lines 26-34), various time frames after imaging (example 5), imaging reperfusion (example 6), etc. The contrast agents include manganese complexes, such as Mn-DTPA, as claimed, etc., see column 6, lines 50-65. Since the contrast agents disclosed by Ericsson are the same as encompassed by the instant invention, i.e., claim 46, such contrast agents (e.g., Mn-DTPA) would be expected to have the same properties as claimed, i.e., K_a values. Ericcson teaches methods which use contrast agents having various additives as set forth in new claims 70-74, including calcium complexes, various salts, ascorbate, etc., see column 8. While the methods disclosed by Ericsson relate to the use of both a positive and negative contrast agent, the instant claims are open-ended, by reciting "comprising" and therefore do not exclude the use of additional contrast agents, as disclosed by Ericsson. Ericsson also teaches that the contrast agents may be administered separately, see column 4, lines 30+ (said separate administration would have the step of "administering to said body a contrast agent consisting essentially

of..." as claimed, since the separate administration would include a step of administering only one of the positive or negative contrast agents. Ericsson also teaches that a single species may be used for both the positive and negative contrast agents, see column 7, lines 12-15.

Response to Arguments

Applicant's arguments filed 8/28/2003 have been fully considered but they are not persuasive.

Applicant asserts that Ericcson differs from the instant invention because the method includes the step of administering a contrast agent consisting essentially of a manganese complex, while Ericcson uses a positive a negative contrast agent.

This is not found persuasive because the claimed method does not exclude additional method steps of administering a contrast agent, as the method recites "said method comprising" in line 2. Thus, the claimed method only limits a step therein to administering a contrast agent consisting essentially of a manganese complex. Ericcson discloses such a step by teaching that the positive or negative contrast agents may be administered separately. Wherein the positive contrast agent is a manganese complex (e.g., claims 6 or 7) the method disclosed by Ericcson would include the step of administering a contrast agent consisting essentially of a manganese complex in a method as claimed. Ericcson also teaches that a single species may be both positive and negative contrast agents, thus, the method would be encompassed by the consisting essentially of terminology. Further, the consisting essentially of terminology does not clearly exclude the negative contrast agents disclosed by Ericcson. For example, the negative contrast agents are metal complexes; however, metal complexes are not excluded from the contrast agent as claimed, as shown by claims 70-74, especially claim 70. Since such additional components can be present in the claimed contrast agents, it is unclear what is being excluded from the contrast agents as claimed. For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising." See, e.g., PPG, 156 F.3d at 1355, 48 USPQ2d at 1355. For the reasons above, the use of "consisting essentially of" does not differentiate over the methods disclosed by Ericcson.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 51-53 and 55-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Edelman (US Pat. 5,492,123) in view of Rocklage (US Pat. 4,889,931).

Edelman discloses a method of detecting myocardial ischemia in a body comprising administering a contrast agent and subjecting the body to MRI to identify regions of abnormal blood flow to detect the ischemia, see column 1 and column 2, lines 25-36. Various MRI methods may be employed, such as echo planar MRI, etc., which would encompass the MRI methods and conditions thereof, as instantly claimed, see columns 1-2 and column 5, lines 37+. Edelman teaches that contrast agents are employed, such as, a Gd-DTPA metal complex, see column 5, lines 32-36.

Edelman fails to disclose the use of the same contrast agents as instantly claimed (e.g., manganese complexes, such as, those of formula I and dosages thereof.

Rocklage discloses MRI contrast agents comprising manganese are superior chelating agents which are highly stable, making them very suitable for methods of MRI imaging, see column 1. Thus, Rocklage teaches that manganese in the preferred metal for such MRI complexes. The contrast agents include manganese complexes of DTPA, DPDP, etc. is especially preferred, see column 4, lines 50+. These chelates are the same as those instantly claimed and are used in dosages which encompass those instantly claimed, see column 9, lines 1+. Since these contrast agents are the same as those instantly claimed, they would be expected to have the same functional characteristics and properties as instantly claimed.

It would have been obvious to one of ordinary skill in the art to modify the methods disclosed by Edelman to use a manganese contrast agent and dosages thereof, as instantly claimed, because such

Rocklage teaches that such contrast agents (e.g., a manganese complex of DPDP, DTPA, etc.) are superior chelating agents which are highly stable, thus, making them very suitable for methods of MRI imaging when used in dosages encompassed by the claims. One of ordinary skill in the art would have been motivated to employ the improved manganese complexes as the contrast agents in the methods of Edelman to gain the advantages Mn complexes, including optimum MRI properties, decreased toxicity, etc., as is known in the art, as shown by Rocklage.

Claims 51-53, 55-58 and 63-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Edelman (US Pat. 5,492,123) in view of Ericcson (WO 95/02831, US 5,869,023 used as a US equivalent).

Edelman discloses a method of detecting myocardial ischemia using a metal chelate and MRI as set forth above.

Edelman fails to specifically disclose the use of manganese as the metal in the chelate and the various modifications of detecting such conditions as set forth in claims 47-50.

Ericcson discloses a method of detecting myocardial ischemia in a subject, as set forth above. Ericsson teaches that Mn is an equivalent metal to Gd (as disclosed by Edelman) and that the methods may be employed for various evaluations of myocardial ischemia, including evaluating severity, reperfusion, injured tissue, etc, see column 6, lines 50-65 and examples 4-6.

It would have been obvious to one of ordinary skill in the art to have used Mn instead of Gd in the DTPA metal complex used in the methods disclosed by Edelman because it is well known in the art that Mn is an equivalent metal to form a complex with DTPA for methods of MRI, as shown by Ericcson. Also, it would have been obvious to one of ordinary skill in the art to employ the methods disclosed by Edelman for various myocardial diagnostic determinations because Edelman teaches general methods of myocardial imaging and methods to identify various subgroups thereof, severity, etc., (as claimed) are well within such general methods and/or are known in the art as shown by Ericsson.

Response to Arguments

Applicant's arguments filed 8/28/2003 have been fully considered but they are not persuasive.

Applicant asserts that there is no reasonable expectation of success for using the contrast agents disclosed by Rocklage or Ericcson in the methods disclosed by Edelman because Edelman does not teach the use of manganese contrast agents.

This is not found persuasive because Edelman provides a general teaching that MRI contrast agents may be employed in the disclosed methods. Edelman does not limit the invention to the use of Gd-DTPA or iron oxide, but only provides these as examples of MRI contrast agents. On the other hand, Rocklage clearly discloses manganese contrast agents as being superior chelating agents for methods of MRI imaging because they are highly stable, less toxic than other paramagnetic metals, etc. Clearly, one of ordinary skill in the art would have been motivated to employ improved or superior MRI contrast agents in the methods disclosed by Edelman which provides a general teaching that any MRI contrast agents may be employed. Obviousness does not require absolute predictability.

Claim Rejections - 35 USC § 103

Claim 54 rejected under 35 U.S.C. 103(a) as being unpatentable over Edelman (US Pat. 5,492,123) in view of Rocklage (US Pat. 4,933,456), as applied to claims 31-33 and 35-46 above, in further view of Goldenberg (US Pat. 5,632,968).

Edelman fails to specifically disclose that the echo imaging is an inversion recovery echo imaging method.

Goldenberg discloses methods of imaging cardiovascular lesions and teaches that inversion recovery is a well known and equivalent method of spin-echo MRI, see column 13, lines 23-48.

It would have been obvious to one of ordinary skill in the art to further modify the methods disclosed by Edelman to use inversion-recovery spin-echo MRI as the spin echo MRI procedure because it is well known in the art that this is a useful and equivalent method of spin-echo MRI as taught by Goldenberg.

Claim 34 rejected under 35 U.S.C. 103(a) as being unpatentable over Ericsson in view of Goldenberg (US Pat. 5,632,968).

Ericsson while disclosing that various known echo imaging MRI modalities may be employed fails to specifically disclose that the echo imaging is an inversion recovery echo imaging method.

Goldenberg discloses methods of imaging cardiovascular lesions and teaches that inversion recovery is a well known and equivalent method of spin-echo MRI, see column 13, lines 23-48.

It would have been obvious to one of ordinary skill in the art to further modify the methods disclosed by Ericsson to use inversion-recovery spin-echo MRI as the spin echo MRI procedure because it is well known in the art that this is a useful and equivalent method of spin-echo MRI as taught by Goldenberg.

Response to Arguments

Applicant's arguments filed 8/28/2003 have been fully considered but they are not persuasive.

Applicant asserts that it would not have been obvious to lower the dose of a manganese complex contrast agent in fast-imaging techniques.

This is not found persuasive because Ericcson teaches the same dosages of contrast agent as claimed (see column 7). There is nothing in Edelman to suggest more contrast agent is needed in fast imaging techniques.

Conclusion

No claims are allowed at this time.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael G. Hartley whose telephone number is (703) 308-4411. The examiner can normally be reached on M-F, 7:30-5, off alternative Mondays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (703) 308-2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Michael G. Hartley
Primary Examiner
Art Unit 1616

MH
10/16/2003